



## Editorial

# The savior of binge drinkers: Another liver tonic from a common vegetable?



## 1. Study of hepatoprotective effect of *Solanum nigrum* in this issue of JCMA

The liver is the organ that metabolizes nutrients and xenobiotics, and it is susceptible to injury by various toxins and metabolites. Alcohol liver disease (ALD) is one of the most common liver diseases around the globe. Although numerous efforts have been undertaken to combat this global health burden, there is no therapeutic modality to date for patients with ALD. In this issue of JCMA, Liu et al.<sup>1</sup> show that aqueous extracts from *Solanum nigrum* have hepatoprotective effects against ethanol-induced liver injury based on *in vitro* and *in vivo* animal models. The study was well-conducted and produced solid results and is the first study about *S. nigrum* focusing on the prevention of alcohol-related liver damage. Since *S. nigrum* is a common vegetable consumed worldwide, we are intrigued as to whether *S. nigrum* can be efficacious as a liver tonic to combat ALD.

## 2. *S. nigrum* as food and herbal medicine

Although parts of *S. nigrum* can be toxic to humans, it has been utilized as food or as a medicinal herb worldwide for thousands of years.<sup>2</sup> The plant has a long history of medicinal usage, dating back to ancient Greece. Additionally, it is a traditional European herb used as a sudorific, analgesic, and sedative with narcotic properties.

*S. nigrum* is also an important herb used in traditional Indian medicine, where it is incorporated into treatments for dysentery, gastrointestinal diseases, and fever. The juice of the plant is also used on ulcers and other skin diseases, and the fruits are used as a tonic, laxative, and appetite stimulant and for treating asthma. *S. nigrum* is a widely used plant in oriental medicine, where it is considered to be antitumorigenic, antioxidant, anti-inflammatory, hepatoprotective, diuretic, and antipyretic.<sup>2</sup>

## 3. Hepatoprotective effects of *S. nigrum*

The protective effects of the aqueous or ethanol extract of *S. nigrum* have been demonstrated in carbon tetrachloride

(CCl<sub>4</sub>)-induced liver injury in rats.<sup>3</sup> The effect of *S. nigrum* extract has also been evaluated on thioacetamide (TAA)-induced liver fibrosis in mice.<sup>4</sup> Histological examination suggested that *S. nigrum* can reduce the degree of fibrosis caused by TAA treatment.<sup>4</sup> *S. nigrum* can also decrease cadmium chloride (CdCl<sub>2</sub>)-induced hepatotoxicity in rats.<sup>5</sup> These studies suggest that *S. nigrum* could protect the liver against CCl<sub>4</sub>-, TAA-, and CdCl<sub>2</sub>-induced liver injury in rats. Hepatotoxicity induced by different toxins may have some common pathways, but differences still exist between them. Ethanol-induced liver injury seems more complicated than toxin-related hepatic damage. A two- or three-hit theory has been proposed as the pathogenesis of ALD and nonalcoholic fatty liver disease. However, there had been no published study about the cytoprotective effect of *S. nigrum* against ALD until Liu et al.'s<sup>1</sup> article was published in this issue of JCMA.

## 4. Merit of Liu et al.'s<sup>1</sup> study

This is a well-designed controlled study using mice and hepatocytes harvested from mice as the *S. nigrum* therapeutic targets to prevent ethanol insult.<sup>1</sup> Multiple biomarkers of hepatocyte injury were used to assess the hepatoprotective effect of *S. nigrum*. These included alanine aminotransferase (ALT), aspartate aminotransferase (AST), malondialdehyde, superoxide dismutase, glutathione peroxidase, and glutathione S-transferase A1 (GSTA1).<sup>1</sup> It has been shown that *S. nigrum* has the dose-effective capacity to mitigate the hepatocyte damage presented in all biomarkers, in addition to evidence of histology of the liver. The result of this study is crucial in the elucidation of the underlying mechanism of *S. nigrum* in relation to its hepatoprotective effect against ethanol. The authors emphasized that GSTA1 can be an early predictor of hepatocyte injury, compared with the conventional tests of liver enzymes ALT and AST.<sup>1,6</sup> The role of GSTA1 in the early detection of liver injury is intriguing in the field of drug-induced liver injury (DILI) since the application of genetic markers and other biomarkers of DILI is time-consuming and they typically have low sensitivity and specificity.<sup>7</sup> However, relevant articles about GSTA1 in acute liver injury are scarce,

and further studies to validate its value in clinical application are warranted.

## 5. Limitations of this study

Although Liu et al's<sup>1</sup> study has demonstrated the mechanism and potential hepatoprotective role of *S. nigrum* in ethanol-induced liver injury using the hepatocyte and mice model, is it time to encourage consuming more *S. nigrum* as a liver tonic before an alcohol binge? The answer is no. Hundreds of vegetables and herbs have been shown to have some hepatoprotective effects in earlier studies of cytomolecular levels and animal models. However, no one vegetable or herb has efficacy in the diverse liver diseases, such as chronic hepatitis B, chronic hepatitis C, and alcoholic hepatitis. There is still a wide gap between the circumstances of a bench study and clinical application in the biopharmaceutical science community and industry. Accordingly, virtually all medicinal herbs cannot be successfully demonstrated to have proven efficacy and safety as an authentic drug.

Furthermore, aqueous extracts from *S. nigrum* purchased from Harbin Jiacheng Science and Technology Development Co. (Harbin, China) were used in the present study.<sup>1</sup> However, no further details about the components of these aqueous extracts were described. *S. nigrum* possesses various compounds responsible for diverse activities. The major active components are glycoalkaloids, glycoproteins, and polysaccharides, but *S. nigrum* also contains polyphenolic compounds, such as gallic acid, catechin, protocatechuic acid, caffeic acid, epicatechin, rutin, and naringenin.<sup>2</sup> The glycoalkaloids include solamargine, solasonine, and solanine, which belong to the tropane group of compounds. In fact, the function and activity of solanine have been extensively studied, and it is found to comprise 95% of the total alkaloid concentration present in the *S. nigrum* plant.<sup>2</sup> Whether the hepatoprotective effect in this study is from the crude extract or from just one component of *S. nigrum* is unknown. This is the major drawback of this kind of biopharmaceutical study.

## 6. Toxicity of *S. nigrum*

Most species in the *Solanaceae* family may be poisonous to humans as well as to livestock.<sup>2</sup> Although *S. nigrum* is considered to be an edible plant, its toxicity is mainly due to the presence of solanine, a glycol-alkaloid causing varying degrees of toxicity in a dose-dependent manner.<sup>2</sup> Most of the presented toxic symptoms/signs are the anticholinergic effect of alkaloids, including nausea, vomiting, diarrhea, headache, dizziness, slurred speech, fever, sweating, tachycardia, dilation of pupils, blindness, mental confusion, convulsions, coma, and even death.<sup>2</sup> The amount of toxic alkaloid in a plant depends on the climate, soil type, season, and maturity. The green unripe berries are generally considered more toxic than the ripe berries.<sup>2</sup> Therefore; it is probable that by boiling the plant, the toxic components are destroyed given that the plant is reported to be edible after cooking.

In conclusion, *S. nigrum* is a widely used plant incorporated into herbal medicine and food and possessing various characteristics, such as antitumorigenic, antioxidant, anti-inflammatory, hepatoprotective, and antipyretic activity. Liu et al's study<sup>1</sup> as referenced in this issue of JCMA used *in vitro* and *in vivo* mice models to assess the hepatoprotective effect of *S. nigrum* on ALD. They found *S. nigrum* can protect the integrity of hepatocytes and thus reduce the release of liver GSTA1. However, it is still premature to suggest the consumption of *S. nigrum* as a liver tonic to prevent alcohol hepatitis because of the potential anticholinergic toxic effect of this plant and the lack of evidence or clinical data to validate its efficacy and safety in ALD. Boiling this vegetable is suggested to avoid toxicity. However, to examine a more expanded clinical application of *S. nigrum*, this plant with its wide-ranging therapeutic properties needs to be investigated in well-designed clinical studies.

## Conflicts of interest

The author declares that he has no conflicts of interest related to the subject matter or materials discussed in this article.

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